Guest Editorial
The Biomedical Imaging Resource At Mayo Clinic

I. Introduction

THIS editorial will review the history and summarize achievements, describe current activities, indicate future directions, and finally suggest some keys to success of the Biomedical Imaging Resource (BIR) at Mayo Clinic/Foundation. The origin and history section provides a chronological description, with associated references, emphasizing progress and milestones over the past three decades. Several figures are included to illustrate and highlight some particularly unique achievements.

II. Origin and History

1970–1980

It is difficult to pinpoint a specific time when the roots of the BIR first took hold. It has been a continuous evolution over many years. But the early 1970s is selected as the starting point for this review since that is when I began my professional career at Mayo Clinic. At that time, we were basically known as "Wood's Group." This was a familiar reference to Dr. Earl Wood and those who worked in his laboratory. Dr. Wood had recruited several young investigators from both the biological and physical sciences. Four of these budding scientists (Erik Ritman, Jim Greenleaf, Barry Gilbert, and myself) are still at Mayo Foundation, each with laboratories and active research programs of their own. Others who joined Dr. Wood's laboratory during this decade and made important contributions were Steven Johnson, Jim Kinsey, Eric Hoffman, Peter Chevalier, and Lowell Harris. Several visiting scientists also made seminal contributions, including Gabor Herman and Y. C. Pao. Dr. Wood had assembled and trained a competent staff of skilled technicians and allied health professionals (notably Ralph Sturm) which made his laboratory one of the truly unique and progressive facilities in cardiovascular physiology research.

In the late 1960s, "Wood's Group" had begun looking at ways to quantitatively analyze video fluoroscopic images, primarily of the heart, lungs and circulation [1]. When I joined the group in 1972 on a National Institutes of Health (NIH)-funded postdoctoral fellowship, one of the first projects I engaged was to develop a way to digitize video images. A quite unique system, perhaps the first of its kind, was designed and built to digitize successive video frames from a stop-action video disc or camera [2]. The early 1970s also marked the advent of medical computer-assisted tomography when the first CT scanner for head imaging was announced [3]. We became interested in applying this new cross-sectional imaging technique to three-dimensional

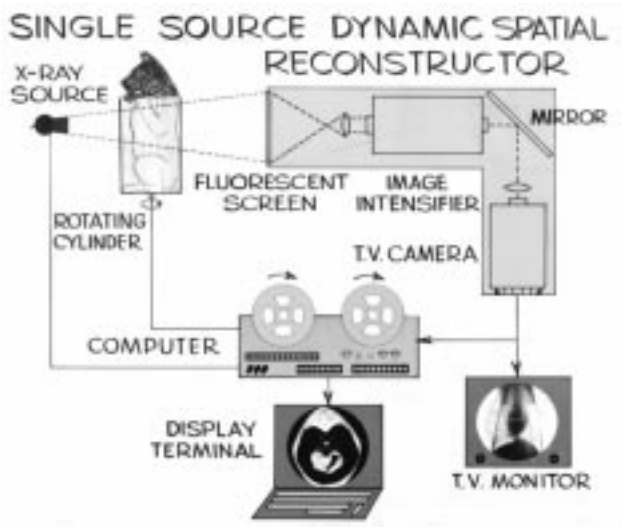

Fig. 1. Diagram of Mayo SSDSR, first experimental volume CT scanner designed in 1973, based on digitized multiplanar video fluoroscopic images obtained by rotating the subject within the field of view.

(3-D) imaging of the heart and circulation, a goal Dr. Wood had been pursuing using computerized bi-plane fluoroscopy for a number of years [4]. This active interest resulted in the design and construction of an unique experimental 3-D scanner called the single-source dynamic spatial reconstructor (SSDSR) (Fig. 1). The key to this system was to use each digitized line from multiplanar video fluoroscopic views (using the aforementioned video digitizer) to reconstruct many parallel adjacent cross sections of the imaged regions of the body, producing a 3-D volume image. This 1973 SSDSR system was the first CT-based scanner to produce volume (3-D) image scans (Fig. 2) of experimental animals [5], including the first dynamic volume scans of breathing lungs (Fig. 3) and beating hearts (Fig. 4) in the intact chest [6]. These experiments demonstrated, for the first time, the possibilities of dynamic volume 3-D reconstruction [7] which was only to become available in commercial scanners more than a decade later. Several versions of 3-D reconstruction algorithms were developed to accommodate the cone-beam image projection data produced by the SSDSR [8], [9].

The video digitizing system produced another milestone in the early part of the decade; namely, the first digital subtraction angiogram (DSA) [10]. Using electrocardiogram-gated images of the heart, video frames from the same point in the cardiac cycle recorded before and after injection of X-ray contrast material into the coronary arteries could be digitized and subtracted, highlighting the contrast-media-filled coronary vessel tree (Fig. 5). These unique video digitizing and computing capabilities enabled several new applications and fostered new image research collaborations for the laboratory that had not been possible before, including video densitometric analysis of

Publisher Item Identifier S 0278-0062(01)07783-7.

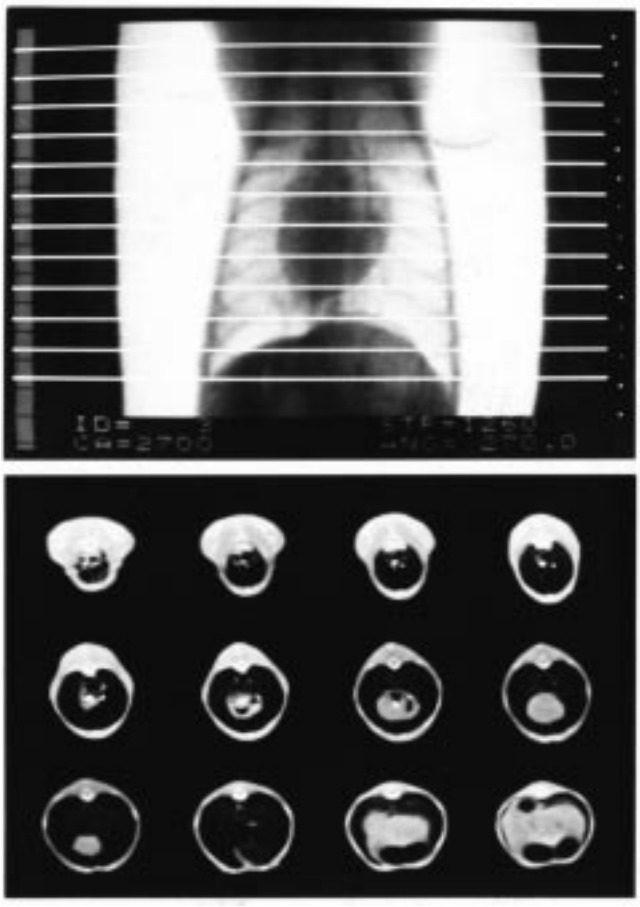

Fig. 2. First volume image reconstructed of dog chest from Mayo SSDSR in 1973. Each line in video fluoroscopic image (top) was digitized at multiple angles of view around 180° and used to reconstruct a "stack" of up to 250 1-mm-thick adjacent cross-sectional images (bottom).

bone porosity [11], [12], nerve morphometry [13], and analysis of metaphase spreads of chromosomes for automated digital karyotyping and 3-D reconstruction [14], [15].

With the experience (and confidence) gained with the SSDSR, a truly dynamic spatial reconstructor (DSR) was designed, featuring a rotating gantry with multiple X-ray sources and multiple video cameras [16]. After three large grant applications and site visits, the National Heart, Lung, and Blood Institute (NHLBI) in 1975 funded construction of the DSR [16]–[18]. SSDSR experiments continued throughout the decade while the DSR was being manufactured. With the successful completion and installation of the DSR in 1979 (Fig. 6), the first truly dynamic synchronous 3-D volume images of the full chest (Fig. 7) and intact lungs and beating heart (Fig. 8) were obtained and published [19], [20]. Specialized algorithms for 3-D image processing, display, and analysis were developed, including 3-D renderings that could be mathematically "opened up" to give 3-D views inside the heart [21], [22]. Such images (Fig. 9) were early forerunners of virtual endoscopy, which was not "invented" until the early 1990s (more on this later).

So, during the decade of the 1970s, the nascent BIR developed a significant portion of the early computing resources and capabilities required for dynamic spatial reconstruction, visualization and analysis of dynamic volume image [four-dimensional (4-D)] data produced by the NHLBI-funded SSDSR and DSR. In parallel, the Mayo Biotechnology Computer Resource (BCR) Center, which I headed since 1976, enjoyed continual grant funding from the Division of Research Resources (DRR) at NIH to help support and sustain these same developments, particularly the computing requirements. A relatively powerful mainframe computer was at the heart of the Center and provided virtually all of the computing for the SSDSR and DSR. These two NIH institutes (NHLBI and DRR) were the primary sources of funding for many exciting achievements, some first in the field, throughout the 1970s and 1980s. One measure of the recognized impact of the several unique accomplishments associated with the DSR—its successful design and development, diverse applications and associated computational advances—is provided by two reviews in prestigious journals published at the end of the decade: one in *Radiology* [23] and one in *Science* [24].

1980–1990

In the early 1980s, "Wood's Group" became known successively as the Biophysical Sciences Unit (BSU) and then the Biodynamics Research Unit (BRU) [25]. The BSU designation was short-lived, but the BRU, initially headed by Dr. Wood, was to flourish under the direction of Dr. Erik Ritman, who replaced Dr. Wood and also took over as principal investigator on the NHLBI program project grant which supported the DSR. I continued as head of the BCR and as principal investigator on the DRR resource center grant. These two sources of funding and the projects they supported blended together throughout the 1980s to produce evolutionary advances, including careful characterization of the performance of the DSR [26], [27] and development of efficient algorithms and special-purpose processors to transfer, compute, and display the large-volume image datasets that the DSR produced [28]–[31]. The DSR began to be used in a variety of research and clinical applications, and over 300 patients were scanned during the 1980s [32]–[36]. By the middle of the decade two books had been published documenting much of the early success of the DSR and associated computational facilities [37], [38].

By the middle of the decade, it became clear to me that large-scale mainframe computer systems were not the best way to process and deliver medical images for visualization and analysis. There were no workstations available at that time, so the BCR undertook to develop a workstation from scratch. It was based on a Charles River Data Systems 32-bit processor, augmented with one megabyte of memory (large for the time), a tablet input device, and a graphic display [39]. The system also featured a unique 3-D display device (Fig. 10) based on a computer controlled vari-focal mirror [40]. New image processing functions, faster algorithms, and software modules tailored to efficiently address the computational demands for visualization and analysis of an ever-increasing volume of 3-D and 4-D image datasets continued to be produced at a rapid pace [41]–[43].

It was at this same time (about 1984–1985) that my colleagues and I came to the realization that the several separate software algorithms, routines, and modules that were being used to reconstruct, display, process, edit, and measure the

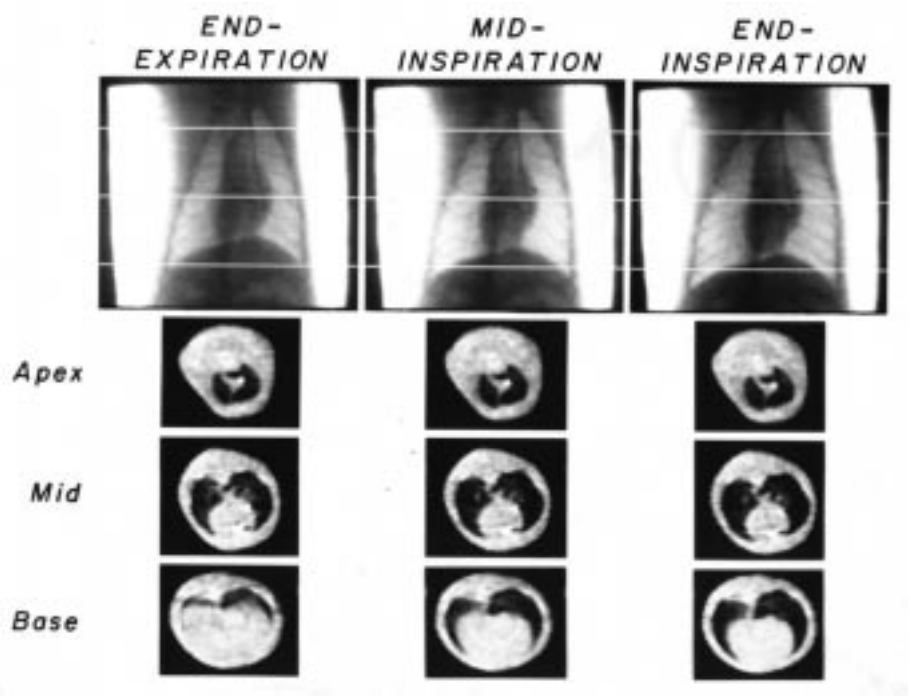

Fig. 3. First dynamic volume image of dog chest reconstructed from Mayo SSDSR in 1973 showing cross sections at three different anatomic levels of chest and at three different times in the respiratory cycle. Gated imaging was used, i.e., one complete respiratory cycle was recorded at each angle of view and time-points in each view subsequently matched for reconstruction.

DSR volume images would be more beneficial to the user if they could be combined into one efficient program with a common interface to all modular processes and on-line access to the original and processed datasets for interactive viewing and analysis. This idea gave birth to "*Analyze*" [39], [43], a comprehensive software system developed to synergistically integrate the best of the various computer programs that had been separately developed up to that point, each of which could be quickly accessed by an easy to use graphical human interface (Fig. 11).

These two fundamental developments in the early 1980s, the design and assembly of a special purpose workstation and the development of the Analyze software system, characterize the imaging research philosophy [43] of the BIR that has prevailed since that time; namely, *what is required to do useful research with biomedical images is an integrated, interactive, and extensible software package installed on individual workstations and PCs*. The software should also permit automatic import of "raw" images produced by evolving new scanner systems, such as magnetic resonance imaging (MRI), positron emission tomography (PET), and 3-D ultrasound (US). In accord with this philosophy, the Analyze package was first ported to a desktop personal computer [44] in the late 1980s, featuring its own custom graphic user interface (i.e.,—not Windows, yet!).

By the late 1980s the BCR became administratively known as the BIR, both within Mayo and externally. The BIR had developed considerable experience and unique expertise in image processing and imaging science to help other investigators at Mayo, and also had entered into many successful extramural collaborations around the world. Analyze was disseminated to these other imaging scientists to help them in their imaging research. They in turn provided useful input for improving Analyze and expanding its applications. Such collaborative uses of Analyze are often published with co-authorship from the BIR [45]–[47]. In addition to dissemination to academic collaborators, Analyze began to be

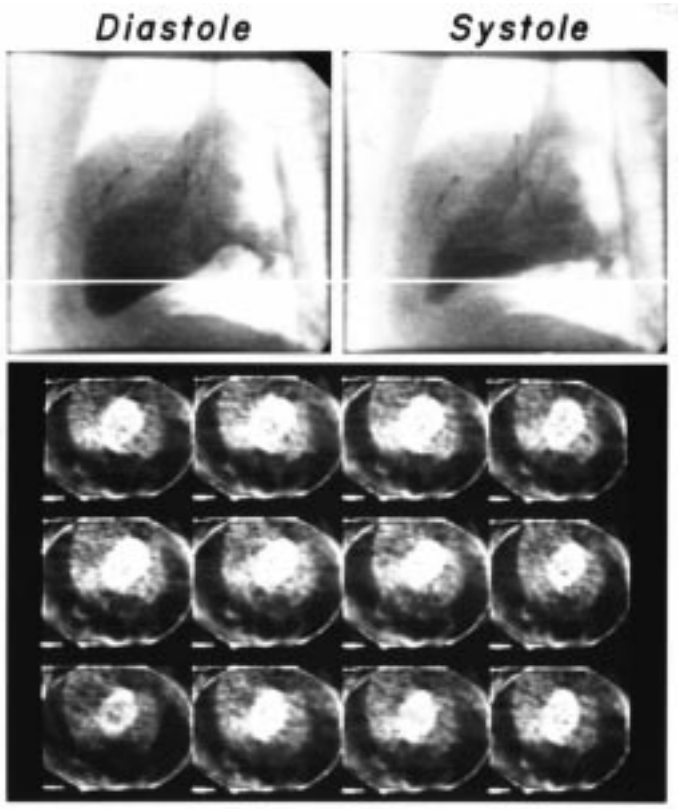

Fig. 4. First dynamic volume image of beating heart intact within dog chest produced by Mayo SSDSR in 1973. Gating on the ECG was used to record video projections (top) while contrast material was injected into left ventricular chamber. Shown is a single cross section reconstructed at 16 successive points through one complete heart cycle. Bright contrast region is left ventricle.

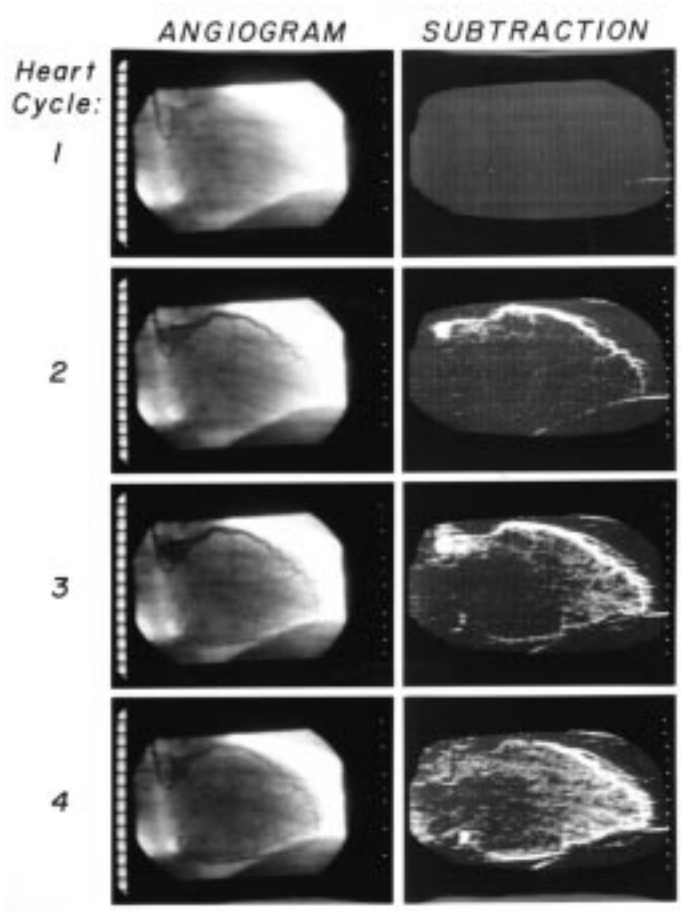

Fig. 5. First DSA obtained in 1973 from Mayo video digitizing system. Video images at same point in cardiac cycle before and after injection of contrast material into coronary arteries were digitized and subtracted. The difference images reveal the coronary vessels and the blush of perfusion in the myocardium in successive heart cycles.

Fig. 6. Photograph of Mayo DSR after installation in 1979, the first multisource, multidetector volume CT scanner. The system design featured 28 X-ray tubes, a curved fluorescent screen, and 28 high-performance lenses and video cameras mounted on a gantry (bottom) that weighed 15 tons and rotated at 15 rpm around the subject positioned on the table (top).

successfully licensed to individual companies and independent vendors for commercial distribution. Over time, several major companies and independent distributors have licensed Analyze and made it available around the world. The software has continued to be refined, updated, extended, and, most importantly, fully supported by the BIR for all academic collaborators, as well as for all commercial vendors.

Near the end of the decade, publications about Analyze and the use of Analyze were becoming common, both from the BIR and from many of its extramural collaborators. A particularly important publication titled "*Interactive Display and Analysis of 3-D Medical Images*" [48], which described the fully interactive and feature-rich volume rendering algorithms (Fig. 12) and 3-D image editing and measurement capabilities of Analyze, was awarded recognition more than a decade later as an enduring "classic paper in the medical imaging literature" [49], and has been cited in numerous publications. Other publications from the BIR soon followed to further extend the acceptance and recognition of Analyze as an important contribution to the field [50], [51].

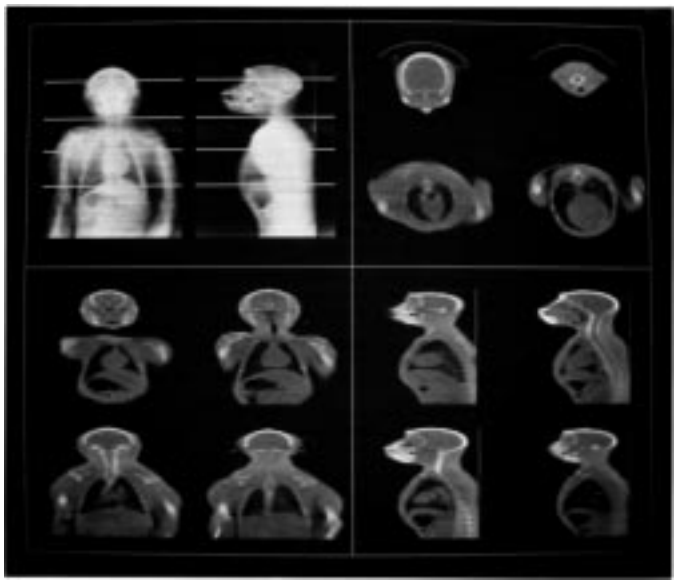

Fig. 7. Early volume CT image from the DSR, showing 3-D reconstruction of a Rhesus monkey, with 1-mm-thick transaxial, coronal, and sagittal sections displayed at four different anatomic locations.

1990–2000

By the early part of the decade of the 1990s, Analyze was well established as one of the premier visualization tools for 3-D image display and analysis. The significant number of mensuration functions in the Analyze package that could be inter-

actively applied while editing, updating, and viewing 3-D renderings of volume images was particularly useful to investigators and clinicians alike. The academic collaborations continued to provide significant and useful input to the Analyze development team to improve and extend the capabilities of the software. Publications came out describing applications in computer-aided surgery [52], [53] and virtual endoscopy [54]. We believe the first paper in virtual angioscopy was published in the early 1990s [55] using Analyze with intravascular US. We also began developing new algorithms for image registration (Fig. 13), one of which was awarded a patent for conceiving and evaluating a new surface matching method using Chamfer distances [56], [57]. The challenging problem of 3-D image segmentation (Fig. 14) was pursued with new algorithms based on multispectral feature and morphologic shape analyses [58]–[60]. A unique application of Analyze occurred in the early 1990s when it was used extensively for planning surgical separation of two pairs of conjoined twins (Fig. 15) at Mayo Clinic [53]. Another book was published [61] describing the "principles and practice" of 3-D biomedical imaging, drawing largely on Analyze and its use with the DSR and with the burgeoning new 3-D CT, MRI, PET, single photon emission computed tomography (SPECT), US, and microscopy imaging systems. By this time, Analyze had "a life of its own" outside of Mayo Clinic and was facilitating numerous research and clinical investigative applications [61].

During the early part of the decade, virtual reality (VR) technologies and applications using interactive simulation of medical/surgical procedures began to be investigated in the BIR. Advanced 3-D visualizations, haptic input, and immersive environments featuring surgery planning/rehearsal procedures were incorporated into a set of routines called VR-assisted surgery program (VRASP) [62]. Prospective clinical applications were tested for specific organ systems in the body, especially computer-aided surgery planning for the brain and the prostate gland [63], [64]. Important new algorithms were developed for efficient production of patient-specific anatomic models computed from segmented volume images obtained from CT and MRI scans [65]. Another important milestone in the history of the BIR came in 1994 when it became the first laboratory to receive the Visible Human Dataset [66], [67] produced by the National Library of Medicine. Immediately the BIR began using this dataset to further validate [68] its many 3-D image processing and display algorithms, especially those used for virtual endoscopy (Fig. 16).

By the middle part of the decade, it was clear that the ten-year-old user interface in Analyze was not an optimal match for the rapidly increasing capabilities of workstations, especially PC systems running the ever more powerful Windows operating system. So the BIR undertook to completely redesign the graphical user interface, while also re-coding all algorithms and image processing functions in Analyze for optimal performance. This effort took two years by a staff of five talented programmers working full time. The result was an extensible library of over 500 optimized image processing functions and routines and a well-defined application programmers interface (API) upon which Analyze could be rebuilt and easily extended. This library was called AVW, for "A Visualization Workshop." AVW, like Analyze, became a popular product disseminated and supported by the BIR to extramural collaborators and also licensed to commercial vendors. By 1995, the "new" Analyze built on AVW using the API was successfully ported [69] to personal computers running under the popular Windows operating system (Fig. 17). The BIR continued to support UNIX (and later LINUX) versions of Analyze for all popular workstations. These developments significantly increased the demand for and usefulness of Analyze for both researchers and clinicians. By the year 2000, Analyze had been installed in over 300 institutions around the world.

All through the 1990s, continued algorithm improvement and refinement were carried out, as well as several important new algorithms developed and incorporated into Analyze [70]–[74]. A number of compute-intensive algorithms (e.g., volume rendering, sync interpolation, enhancement filters) were modified for multithreading and parallel processing, increasing performance several-fold on systems with multiple CPUs [75]. A growing number of diverse applications of the software were initiated and published in the scientific and medical literature [76]–[83]. A particularly exciting clinical application was developed at Mayo Clinic, called SISCOM [84], which provided registration and fusion of 3-D SPECT difference images registered to MR images for image guided surgery planning in treatment of epilepsy patients with debilitating seizures (Fig. 18). This Analyze-based procedure is currently used several times each week on patients at Mayo Clinic and in several other institutions around the world. A brain atlas developed at Kent Ridge Digital Laboratories (Singapore) was incorporated into Analyze to help imaging scientists and neurosurgeons in mapping brain functions and in planning brain resections [85]. Analyze became increasingly used in microscope studies and 3-D reconstruction of histologic sections [86], [87]. A new method [88] developed for 3-D reconstruction and analysis of microvessel patterns demonstrated significant potential for early detection and characterization of prostate cancer (Fig. 19). A new imaging technique was developed [82] for interactive image guided treatment of prostate cancer. It was called transurethral ultrasound (TUUS) and demonstrated significant potential for imaging of the prostate and associated structures (Fig. 20), both preoperatively and intraoperatively. TUUS image-guidance may improve accuracy and specificity of biopsies and provide greater precision in localizing radioactive seeds in prostate cancer brachytherapy [89].

By the end of the decade yet another book was published, which summarized the important developments in and applications of biomedical imaging, visualization and analysis that had been carried out in the BIR over the past decade [90]. Facing the new millennium, the BIR was poised to make further advances in volume image visualization and analysis, and to harvest the results of several important academic and clinical collaborations focused on bringing image-guided, minimally invasive procedures out of the laboratory into clinical practice. These will be further described in Sections III and IV, but first a brief summary of achievements by the BIR over the last 30 years is provided.

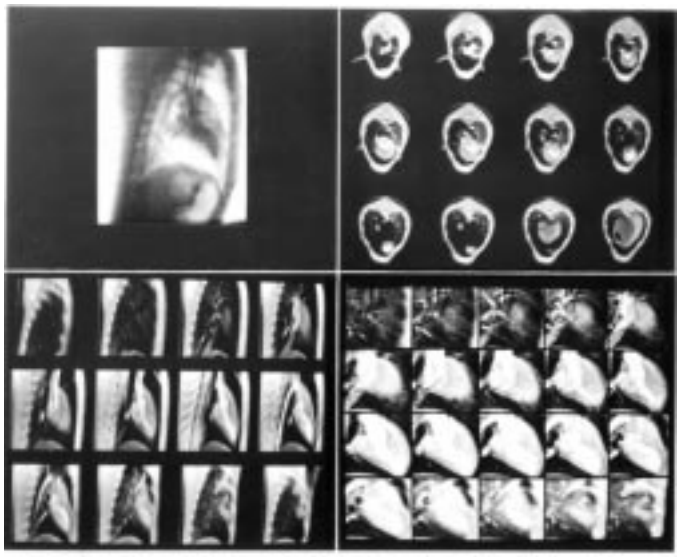

Fig. 8. First 3-D reconstruction of intact lungs and beating heart obtained from the Mayo DSR during a single cardiac cycle (i.e., no gating was used). Zoom-in reconstructions (bottom-right) proceed sagittally through the heart at one time point to reveal the dye-filled left ventricle.

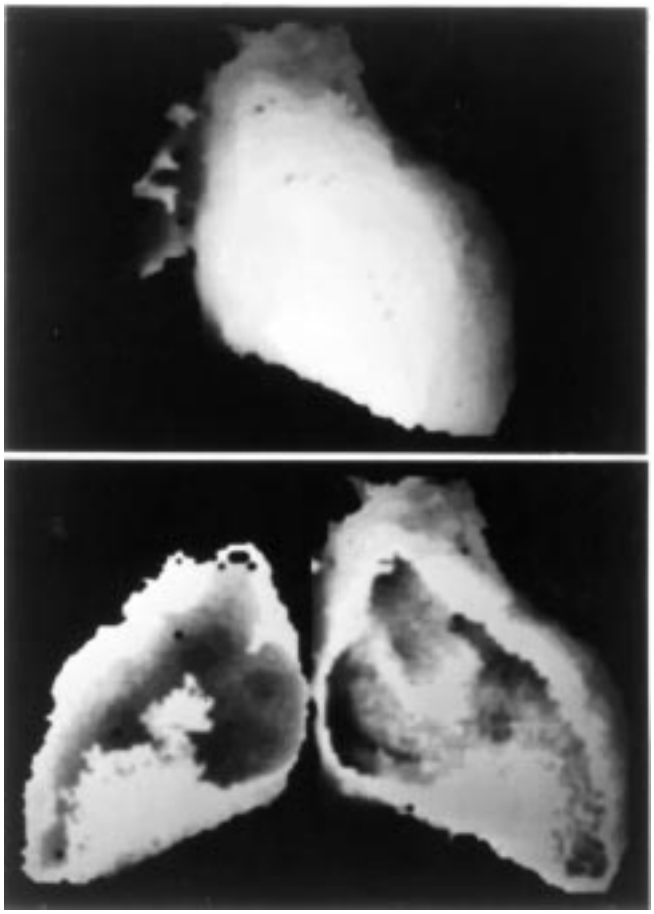

Fig. 9. Three-dimensional surface display of segmented heart (top) computed from patient with common ventricle scanned in the DSR. Bisection (bottom) reveals interior common chambers separated by partial septum. Dynamic sequences of such images displaying multiple interior views of anatomic organs obtained from DSR scans were the forerunner of virtual endoscopy.

Fig. 10. Photograph of first workstation showing operator, keyboard, pointing device, graphic screen and 3-D varifocal mirror display. System was designed and constructed by the Mayo BCR in 1985.

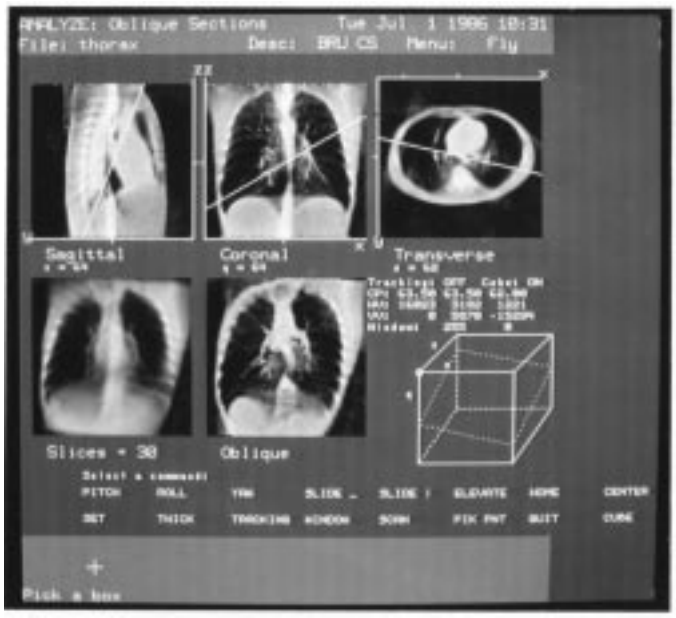

Fig. 11. Photograph of graphical interface on workstation screen showing oblique sections computed from volume image in first version of Analyze in 1985.

Summary of Achievements Over Three Decades

The BIR has been responsible for developing some of the earliest (1970s) capabilities for digitizing X-ray video fluoroscopic images, for developing digital subtraction angiography and for

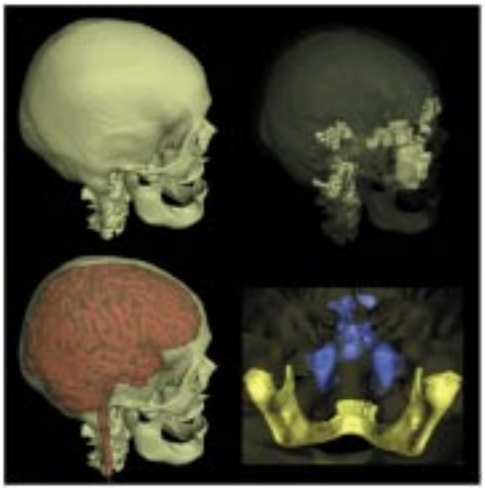

Fig. 12. Photograph of Analyze volume rendering of head showing interactive capabilities for rendering individual segmented objects, multiple objects using transparency, and interior views within volume, all from the same CT scan volume.

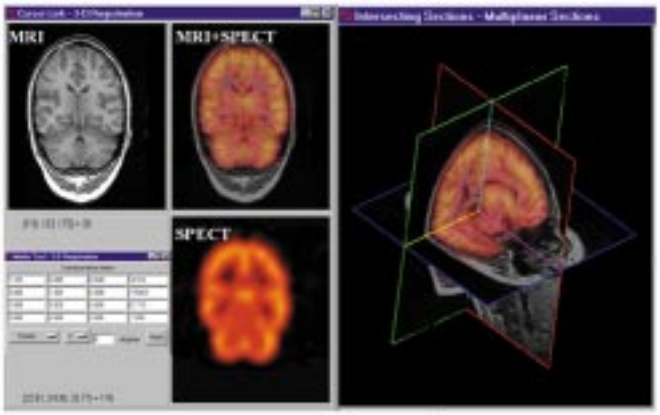

Fig. 13. 3-D registration of MRI and SPECT scans using Analyze, showing original and fused image sections, including intersecting fused orthogonal sections.

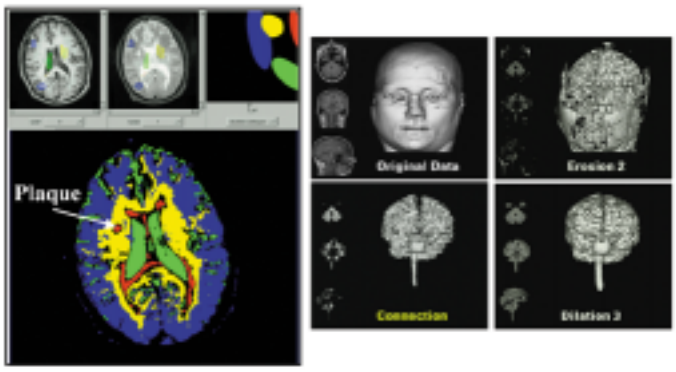

Fig. 14. Multispectral tissue classification (left) and 3-D morphological segmentation (right) with Analyze. T1- and T2-weighted MR images of patient with multiple-sclerosis were used to classify brain tissues and plaques, which can be observed in the white matter. Entire brain can be automatically segmented in a few seconds using math morphology.

developing synchronous dynamic volume scanning CT techniques and systems. The DSR was truly the first multisource, multidetector dynamic volume CT system ever designed, manufactured and used. Development of an individual workstation

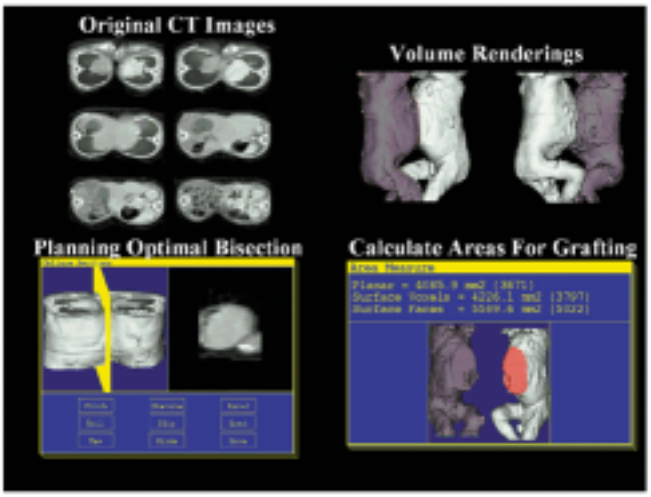

Fig. 15. Composite illustration of procedure to separate conjoined twins as planned with Analyze in 1991. (top left)Multiplanar sections and (top right) 3-D volume renderings, plus editing tools and surface area measurements, were used to select (bottom left) optimal dissection plane and to compute areas of surgical openings (bottom right) to be grafted after operation.

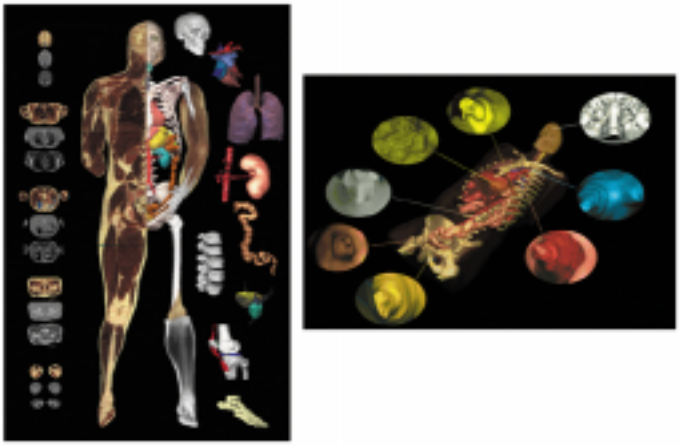

Fig. 16. Illustration of use of Visible Human Dataset to create specific anatomic models (left) and generate virtual endoscopy sequences in many regions of the body (right). Accuracy can be evaluated using the associated true anatomic sections.

with associated 3-D display was among the first of such efforts in the early 1980s. The development of Analyze, a comprehensive, integrated, interactive software program for visualization and analysis of biomedical images, which has continued unabated since 1985 with continued upgrades, dissemination, support, collaboration and commercial licensing, appears to be a singular accomplishment for an academic research laboratory. The capabilities of Analyze to interactively, selectively, and synchronously display, edit and (importantly!) measure multiple image volumes empowered its users beyond any previous capability [90]. Analyze is currently estimated to be installed on over 3000 computers in more than 300 institutions with up to 5000 users around the world. A list of other notable "first" achievements in the BIR would include: 1) successful application of Analyze to planning the separation of two sets of conjoined twins; 2) one of the first laboratories involved in the development and evaluation of virtual endoscopy; 3) development of the SISCOM procedure for image-guided brain surgery

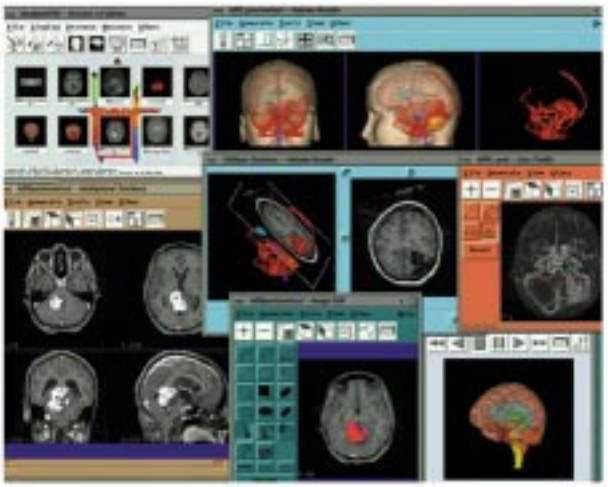

Fig. 17. Photograph of computer screen showing "modern" Analyze graphical user interface on a PC running Windows operating system. Multiple volume datasets, multiple processes, and multiple windows can be simultaneously handled by this version of Analyze, the fifteenth major update version since its creation in 1985.

planning; 4) development of a full anesthesiology simulation and training system; 5) development of a new technique for imaging the prostate using TUUS; and 6) extending visualization and analysis to study of 3-D images obtained from microscope imaging systems. These accomplishments help illustrate and highlight the role that the BIR at Mayo Clinic has played in defining and promoting the discipline of medical imaging science and its applications over the past three decades, especially as related to interactive visualization and quantitative analysis of 3-D and 4-D (dynamic) volume images.

III. Current Activities

The Mayo BIR is dedicated to the continuing advancement of research in the biomedical imaging and visualization sciences. The BIR continues to expand and extend its services and support of both clinicians and investigators conducting research with biomedical images. This section will briefly summarize these services, functions and projects.

The physical space occupied by the BIR exceeds 6000 square feet. Over 100 modern computer systems are located throughout the facility and in staff offices. A variety of special imaging, display, haptic, multimedia and other devices and equipment are located in five main areas: 1) the compute and file server room which contains two mini-super computers with multiple parallel processors for serving computationally intense applications and for serving image file storage and retrieval, which currently exceeds one terabyte; 2) the workstation center offers 15 modern UNIX workstations and PCs running Windows and Linux with high-resolution printers and scanners readily available on a drop-in basis; 3) the advanced visualization and VR lab occupies the largest space in the facility, features several high-performance graphic systems supporting modeling, virtual environments and comprehensive simulations, includes both large and small display devices (visual workbenches, head mounted displays, retinal scanning displays, stereo shutter glasses, etc.), has a number of input devices (haptic stylus, power gloves, laparoscopic impulse engines, 3-D mice, immersion probes, space balls, etc.), and has installed both magnetic and optical systems for tracking user and/or device position and motion within the

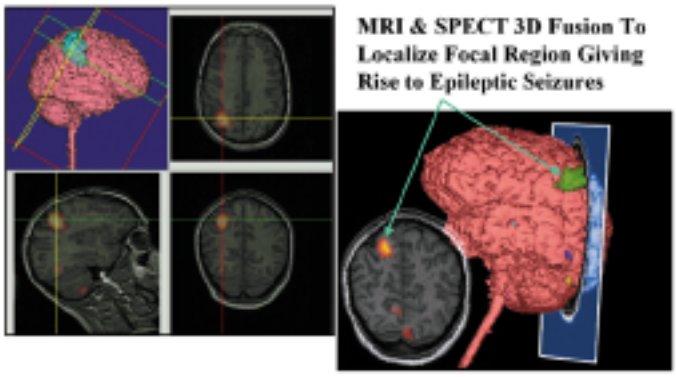

Fig. 18. Subtraction interictal SPECT co-registered to MRI (SISCOM) procedure developed using Analyze at Mayo Clinic for precise localization of brain region to be resected in order to alleviate debilitating seizures in epilepsy patients. 3-D SPECT images recorded during and after seizures are registered and subtracted, the difference images are then registered and fused with a 3-D MRI volume image, and the result is volume rendered to localize the seizure focal region.

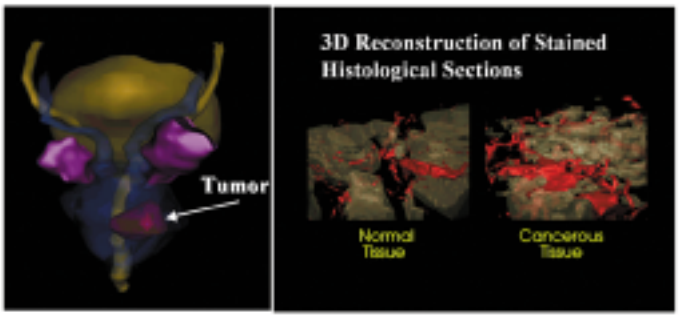

Fig. 19. Three-dimensional segmentation and volume rendering in Analyze of prostate gland with tumor (left) and 3-D reconstruction of stained histologic sections of normal and cancerous prostate tissue (right) excised at surgery. Tortuous and diffuse pattern of microvessels in cancerous tissue can be seen in early (before tumor) angiogenesis, suggesting that this technique may be applied to prostate biopsy samples as a precursor marker for cancer.

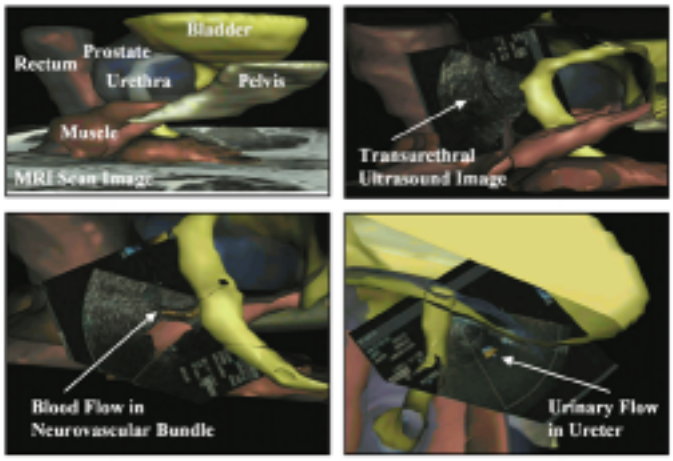

Fig. 20. TUUS images registered to segmented and rendered 3-D model of prostate gland and associated anatomy (top left) computed from 3-D MRI scans. Boundaries of the prostate capsule (top right), blood flow in neurovascular bundles (bottom left, using color flow Doppler), and urinary flow in ureter (bottom right) can be visualized in real time during a procedure.

room; 4) the multimedia lab contains modern all-digital video recording and editing equipment supported by powerful computers for graphic composing, editing and animation, with CD mastering available along with high-resolution color printing, slide generation and movie production; 5) the conference/classroom can seat 25 people comfortably with two full screen displays, computer/graphics support, and all necessary audio/visual equipment for teaching classes in imaging science, giving special demonstrations, and for accommodating seminars, site visits, staff meetings, etc.

The BIR staff is its most valuable resource. Their combined expertise, dedication and creativity demonstrated over three decades of working together continues to provide the research community with efficient, economical solutions and technical support in imaging science. There are 12 full-time engineers, programmers, and technicians in the BIR with an average tenure of almost 20 years. Another dozen, more transient, members of the BIR include graduate students in biomedical imaging and engineering, postdoctoral research fellows and a variety of visiting scientists who come to the facility for various periods of time, extending from one week to one year (e.g., sabbaticals).

The BIR provides a variety of useful tools to research scientists. The advanced visualization and VR lab with its state-of-the-art equipment provides unique capabilities for modeling, simulation and training projects. The major tools, however, are software packages; namely, Analyze and AVW. Currently, over 250 computer systems run Analyze in the Mayo Foundation complex, all supported by the BIR. The BIR also directly supports approximately 50 extramural collaborating laboratories around the world, and provides support for commercial distribution of its software through licensing agreements with several companies. Recent new capabilities in Analyze currently being tested include streamlined modules for virtual endoscopy and surgery planning, an integrated brain atlas, routines for volume digital subtraction angiography and calcium scoring, and a new algorithm for elastic 3-D registration.

Ongoing collaborative projects include development of image guided diagnosis and therapy in coronary artery disease and cardiac electrophysiological abnormalities (Figs. 21 and 22). A complete anesthesia delivery-simulation system has been developed and is being evaluated for training anesthesiology residents. A VR environment and patient interface has been developed to study cataplexy in narcolepsy patients under controlled conditions. A variety of virtual endoscopic applications, including colon and airway, are being developed and evaluated for clinical screening (Fig. 23). Nerve cell analysis, endothelial cell imaging and visualization and measurement of protein folding/unfolding patterns are also current projects using large scale immersive displays in the BIR.

The administration of the BIR is a simple top-down hierarchy. The Director oversees the entire resource and is responsible for its research agenda, academic collaborations, technology development and transfer, intramural service functions and operating budget. The Director has an executive assistant and secretary which support these administrative duties. Three experienced supervisors manage small groups of the staff responsible for: 1) the physical facilities; 2) software development and support; and 3) project coordination, respectively. The staff of program-

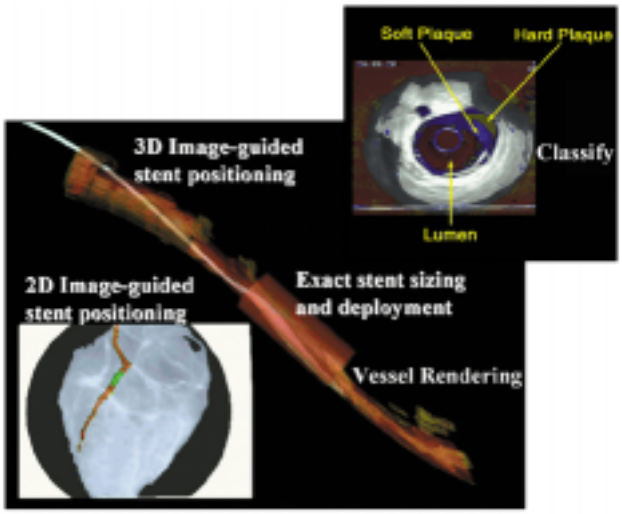

Fig. 21. Illustration of on-line, real-time, image-guided detection and classification of coronary artery plaques and accurate positioning of stent in diseased artery segments reconstructed from intravascular US images.

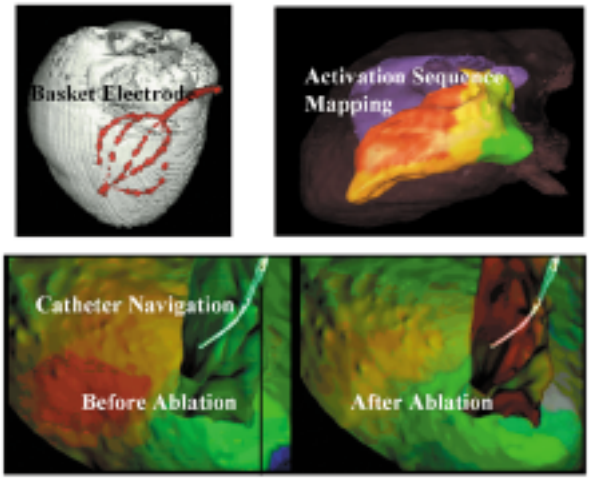

Fig. 22. Procedure for image guided cardiac ablation using 4-D images of the heart obtained from 3-D dynamic CT and/or US scans. Images are fused on-line with electrophysiology recordings from basket electrodes (top left) to localize anatomic regions causing arrhythmia by observing functional activation sequences mapped onto myocardial walls (top right) and navigating to optimal position for focused-energy catheter ablation of the offending region (bottom left), returning cardiac cycle to normal sinus rhythm (bottom right).

Fig. 23. Examples of patient-specific virtual endoscopic images in the colon (left) and airway (right) computed from CT scans. Such images are being evaluated for use in clinical screening.

mers, engineers and technicians are divided among these three supervisory groups, with rotations among them arranged as circumstances dictate.

IV. Future Directions

The BIR continues to advance and improve visualization software for basic research in the image sciences and for image-guided applications in medicine. Next-generation features of this software are expected to include efficient modular procedures for specialized tasks, including radiation therapy planning, on-line augmented reality neurosurgery, life-sign monitoring with retinal displays, and cell and gene analysis. New algorithms will include fast automated elastic registration and rapid automated object segmentation.

The BIR is well-poised to take advantage of new and/or advanced imaging systems. The continually increasing capabilities of 3-D and 4-D medical imaging modalities (CT, MRI, PET, US, etc.) provide powerful new opportunities for medical diagnosis and treatment. However, this potential remains largely unexploited and practical tools undeveloped. The mission of the BIR is to expediently develop, validate, and transfer to practice clinically useful products based on advanced imaging, visualization, and simulation technology. Effective reduction to practice has been a significant part of the history of the BIR—it will play a significant role in its future.

The BIR is committed to realizing the full potential of the VRASP paradigm it has conceived (Fig. 24). Current computer-assisted and image-guided surgery and other clinical procedures are largely relegated to preoperative planning and/or rehearsal on workstations, sometimes in conjunction with immersive 3-D displays. But the greatest potential of advanced visualization technology for revolutionary innovation in the practice of medicine lies in direct, fully immersive, real-time multisensory fusion of real and virtual information data streams during an actual surgical or other clinical procedure. Such technology is under development in the BIR. Some of the most complex and challenging applications, those which show the greatest promise of significantly changing the practice of medical diagnosis and treatment, have begun to be explored in collaboration with Mayo Clinic physicians. These multidisciplinary projects include advanced image-guided, minimally invasive procedures for intraoperative neurosurgery, coronary artery stent placement, quantitative evaluation of coronary plaques, cardiac ablation therapy, focused prostate biopsy and tissue analysis, prostate surgery, prostate brachytherapy, virtual bronchoscopy and colonoscopy, and anesthesia delivery. Preliminary results suggest that in these applications advanced visualization and virtual techniques can provide accurate, reproducible and clinically useful training, patient specific rehearsal, on-line procedures, and minimally invasive interventions. They demonstrate significant promise for improving physician performance, minimizing patient risk and morbidity, and reducing health care costs.

A major goal of the BIR is to integrate and synthesize for visualization and quantitative analysis both structure and function of living objects from image data sets that span a wide range of scale—from molecules and cells to tissues and organs and complete physiological systems. One endpoint of this effort will be to realize "synthetic reality," a virtualization of all

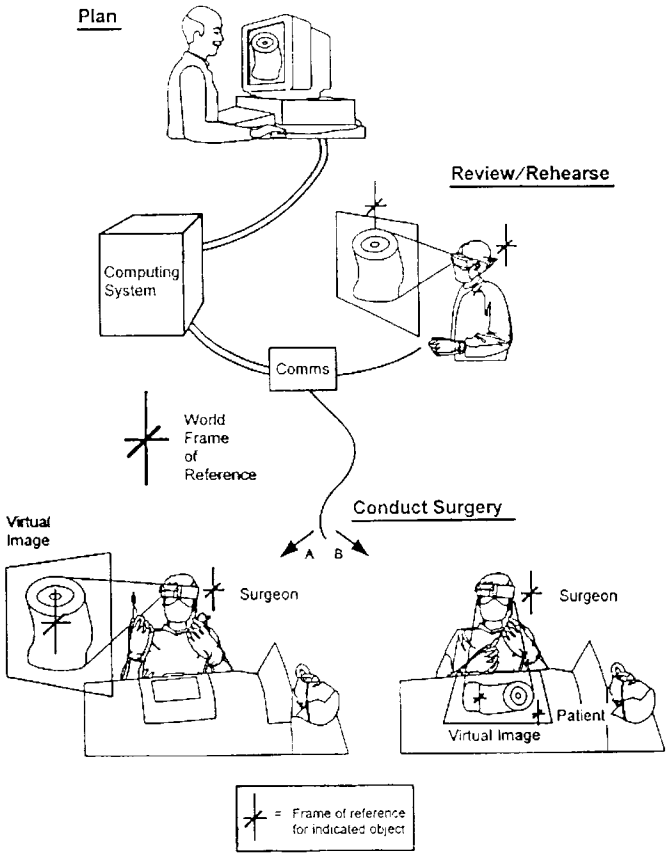

Fig. 24. Diagram of VRASP, a paradigm for evolution of computer/image-assisted surgical or clinical procedures, proceeding from isolated preoperative planning on a workstation (top), to rehearsal on patient-specific data using immersive displays and tactile manipulation devices (center), to on-line, real-time fusion of actual and virtual objects and information during conduct and execution of the surgical or interventional clinical procedure (bottom).

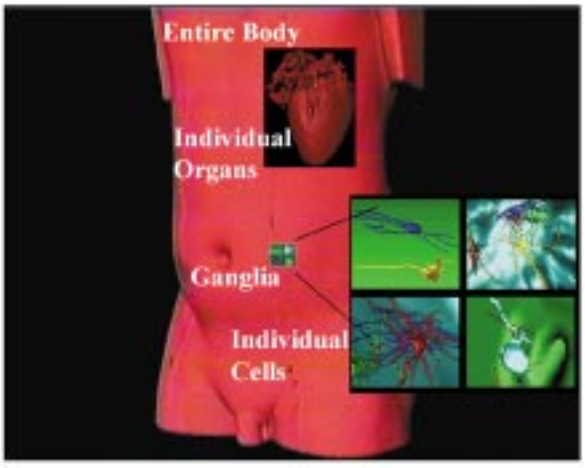

Fig. 25. "Synthetic reality" will permit rapid navigation and detailed exploration of all regions and objects in the body, from entire torso to individual organs to interstitial spaces to single cells, with instantaneous translocation, if desired, and appropriate scaling provided automatically or as selected by the navigator. Physiologic processes may be observed as well, at systemic, organ or cellular levels of detail.

objects of interest, regardless of dimensional size and/or separation, that is sufficiently accurate and faithful so as to render the virtual representations indistinguishable from the real objects. Traversing the distances between these virtual objects and appropriately scaling their local environment to relevant dimensions will be automatic and instantaneous (Fig. 25). Then simulations which teach, train, rehearse, augment or help carry out medical diagnostic, and therapeutic procedures (e.g., telepresence surgery with robots) will become truly useful and ubiquitous. With the expected advances in miniaturization of powerful computing and electronic sensing elements, imaging devices will continue to improve in resolution, speed, and affordability and will be deployed harmlessly within the body, as well as outside of it. Diagnosis and therapy will become synchronous; virtually "one-stop shopping"! The extent to which such capabilities may ultimately be achieved is somewhat speculative, but it is evident that twenty-first-century medicine will represent a culmination of continuing evolutionary developments in multidimensional image visualization and analysis. With ongoing efforts in the BIR and other advanced imaging research laboratories around the world the medical and scientific communities can expect to benefit in improved health care from a continuum of marvelous synergistic advances in imaging, visualization, and analysis technology.

V. Keys to Success

Almost 30 years experience in the BIR at Mayo Foundation has provided me tempered perspective on the key elements required for imaging science groups to be successful and to have enduring impact on the discipline. We have made some mistakes and hopefully have learned from them. We have done some things right and enjoyed modest success. Here are ten key elements to success which have been shaped by our experiences:

1) *Vision:* The leader(s) of imaging science groups need to be able to see the forest and not get lost in the trees. Long-range goals need to be established that are conditioned by a variety of factors, but fundamental to success is pursuing solutions to unsolved problems. There must also be achievable and realizable intermediate aims. An ability to see the need for and make mid-course corrections is often crucial to attainment of the vision, accompanied by a good deal of patience and tenacity.
2) *Convert Ideas to Tools:* Both good ideas and practical working tools are part of a successful enterprise. But ideas are a dime a dozen. This includes patents. Patents, of course, provide "protection," but it is only when reduction to practice of clever ideas happens and effective dissemination and licensing of the technology occurs that broad success can begin to be realized.
3) *People:* A unit like the BIR has benefited from a stable, skilled staff of committed and dedicated engineers and programmers and scientists who have worked together harmoniously over a long period of time, interacting with an ever-changing stream of bright new students, new trainees, and visiting scientists to help define and achieve goals and intermediate aims. I consider the BIR to be somewhat of a national treasure, primarily because of the talented, productive, and experienced staff of the BIR which has been responsible not only for its own success, but has contributed to the success of many others, as well.
4) *Environment:* A supportive institution and administration, with access to facilities and resources, which foster unencumbered research and collaboration with end-users (especially clinicians) is vitally important.
5) *Physical Resources:* Modern facilities and equipment with efficient networking are obvious elements required for successful research and technology transfer in imaging science.
6) *Commitment to "Open-Ended" Development:* This includes commitment to both *de novo* and collaborative development of new technology, and to structuring "products" for extensibility so that refinements are readily achieved and new elements readily integrated over time.
7) *Commitment to Support:* This includes both routine maintenance as well as specialized technical support for users. The BIR staff has directly and continuously supported Analyze since its beginning in 1985, and this support has been largely responsible for insuring that Analyze remained a truly useful medical image visualization and analysis software package.
8) *Funding:* Multiple sources of funding are usually required to make an enterprise like the BIR successful. In our case, these have come from the National Institutes of Health over the years, also from benevolent foundations, and more recently from industry. Mayo Clinic has always generously shared in this support. All of these sources become partners in facilitating relevant basic investigation and technology transfer by research groups.
9) *Collaboration:* This includes both internal and external collaboration. The expertise and capabilities and creativity of the staff of the BIR have been amply demonstrated over its history. But without the life blood provided by new students, new trainees, postdoctoral investigators, visiting scientists, and external academic collaborators there would not be the infusion of new ideas nor the protection against "technological ischemia" nor the insurance of pursuing relevant goals that are required to understand, focus on and address the real needs of basic science and medicine.
10) *Luck:* This would probably be on anyone's list of keys to success. Generally, over such a long period of time as three decades, a certain amount of serendipity occurs whereby the developments, the technology and/or the people just happen to be in the right place at the right time to meet a need and receive recognition. But it is true that chance favors the prepared. So one might anticipate that if the other keys are in place, this key will surely come into play.

Richard A. Robb, *Guest Editor*
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ACKNOWLEDGMENT

In most papers, this section is usually an afterthought, a place to briefly mention those who have assisted or contributed in some minor way to the paper and/or its content. Not so this time. I would like to name here each current member of the BIR at Mayo Clinic and to express my distinct gratitude, admiration and respect for each one of these colleagues who has helped make possible much of the progress in the BIR over the last 30 years, indeed spanning most of my professional career. They are: Kurt Augustine, Bruce Cameron, Jon Camp, Denny Hanson, Ron Karwoski, Mark Korinek, Al Larson, Russ Moritz, Darlene Bernard-Rhude, Margret Ryan, Mahlon Stacy, and Ellis Workman. Thank you one and all. You're great!

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